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No. 8

## THERAPY OF DEAFNESS. REPORT OF CASES.\*

DR. LOUIS GUGGENHEIM, Los Angeles.

#### PART II.

Over 50 per cent of the 18,000,000 deafened in the United States owe their affliction to tympanal pathology resulting from obstruction of the Eustachian tubes in early life.

One of the darkest chapters in otolaryngology is that concerned with the removal of adenoid tissue. The operation is an old one and supposedly a very simple procedure. Because we have been so stupid these many years in taking for granted that our blind adenoidectomy was satisfactorily done, millions of people have been permitted to grow deaf.

Some 30 years ago Joseph C. Beck suggested a direct adenoidectomy by means of elevating the soft palate with a rubber catheter passed through the nose. This was a step in the right direction but the technique was not a satisfactory one. Later, I. D. Kelly presented a modified La Force adenotome through which one could observe that portion of the adenoid which was being removed. It did not give a view of the entire nasopharynx and, therefore, proved unsatisfactory. It remained for Andy Love to present a soft palate elevator which is entirely satisfactory in that it affords a perfect view of the entire postnasal region and permits of the meticulous removal of adenoid tissue under direct vision.

There were more problems, however, which had to be solved. At the end of a year of experimentation with various

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instruments, the necessary ones were finally constructed and the technique of direct adenoidectomy and tubal dilatation was perfected.

My own interest in the neglected nasopharynx was aroused by an experience in 1937, when a hearing clinic was established by Victor Goodhill and myself at the Children's Hospital in Los Angeles. We felt that in a clinic devoted not to diseases of ear, nose and throat but exclusively to the problem of deafness, something new and of value might evolve.

In most otolaryngologic clinics deafness is somewhat of a nuisance because such patients take too much time and after all "nothing can be done for them anyway."

The routine examination at the clinic comprised: 1. a complete history; 2. physical examination of the ears, nose and throat; 3. air and bone audiometery in a soundproof room; 4. voice test; 5. tuning fork test; 6. turning test; 7. direct inspection of the nasopharynx.

The direct nasopharyngoscopy is done with the child flat on his back and without any anesthetic. The entire procedure is explained to the child in advance. This explanation, including the reason for holding feet, hands and head by assistants is psychologically most important. When the soft palate is gently elevated with the Andy Love rectractor a perfect view of the entire nasopharvnx is obtained. According to the statements of children 9 years and older, this procedure is uncomfortable but not markedly painful. After repeated examination by this method, one develops the ability to interpret at a glance the entire condition, including the size of the lateral curtains, the amount of lymphoid tissue in the vault, in Rosenmüller's fossae and covering the orifices of the Eustachian tubes. The child is given water to drink immediately after the examination. It is best to leave the direct nasopharyngoscopy for the last test as very young children may resent it and refuse to co-operate satisfactorily in the other tests.

The picture obtained in this direct examination is totally different from the mirror image or the view through a nasopharyngoscope. The tubal prominences are not seen plainly; the orifices are dimples or slits.

Many of the children examined had had clean tonsillectomies. They rarely had any central adenoid but almost all of them had lateral masses of lymphoid tissue remaining. These masses were in Rosenmüller's fossae and covering the orifices; but in addition, a curtain of lymphoid tissue was found just posterior to each posterior faucial pillar. When the soft palate is elevated these curtains are drawn away from the tubal orifices, but by relaxing the elevator it is noted that the curtains come to lie over them. It is very easy to miss these curtains in performing a direct adenoidectomy.

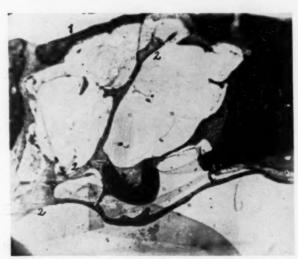


Fig. 1. Web of mesenchymal tissue enmeshing stapes. (1) Footplate of stapes. (2) Mesenchyme.

And so throughout the years we have all deceived ourselves when we removed the adenoid with several insertions of the La Force adenotome, followed with gauze over the finger. We have been leaving the most important part of the lymphoid tissue; that is, most important to hearing.

The histories in all these cases were quite similar. A tonsillectomy and adenoidectomy had been performed. It was noted that the hearing was impaired and growing worse. Back to the doctor for an examination. A look at the retracted drum membranes and the clean tonsillar fossae; a shrug, "nothing to be done now that the tonsils and adenoids have been removed."

In a few cases where direct adenoidectomy had not resulted in a satisfactory improvement in hearing, dilatation of the tubes with the Gerjoye metal olive resulted in further improvement. In a number of cases where no adenoid was



Fig. 2. Fibrous web in oval window niche resulting from mesenchymal differentiation. (1) Footplate of stapes. (2) Fibrous web.

found, the dilatation alone improved the hearing. Thus far, the only explanation for these results is the initiation of tubotympanal mesenchyme resorption.

One never reads the word mesenchyme in otologic literature, and to most otologists mesenchyme is but a name for an embryonic tissue and of no importance whatever to clinical otology.

When I began my special work in Vienna in 1906, one of the first things I learned was that persisting webs of tympanal mesenchyme (see Fig. 1) could, through conversion into fibrous tissue (see Fig. 2), inhibit ossicular movement and produce conduction deafness. With a desire to learn more of this embryonic tissue, I organized a course at the Embryologic Institute, on the ontogenesis of the ear, nose and

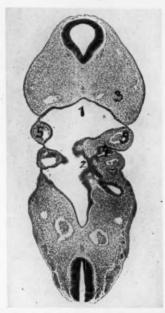


Fig. 3. Human embryo of 4 mm. showing outgrowth of entoderm into cephalic mesenchyme to form pharyngeal pouches and branchial arches (Carnegie Institution collection). (1) Pharynx. (2) Entoderm. (3) Cephalic mesenchyme. (4) Pharyngeal pouch. (5) Branchial arch.

throat. I learned that out-pouchings (see Fig. 3) from the gut into cephalic mesenchyme form the pharyngeal pouches and branchial arches; that the paired first pharyngeal pouches form the Eustachian tubes and tympanic cavities. Gradually this mesenchyme surrounding the primary tube and tympanum is resorbed (see Figs. 4-7) until by the ninth fetal month (see Fig. 8) there is no longer a trace of it. This is the ideal ontogenetic sequence but marked variations in

resorption occur. Many children retain not traces but large amounts of mesenchyme in the tunica propria until the age of 10 or longer. The failure of resorption seems to be an hereditary phenomenon and is very frequently associated with exuberant lymphoid masses in the nasopharynx. This

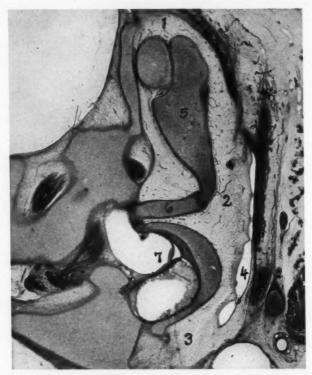


Fig. 4. Section of ear from a three months fetus showing epitympanum, mesotympanum and hypotympanum filled with mesenchyme. Beginning resorption is seen on the right (from the collection of the Carnegie Institution of Embryology). (1) Epitympanum. (2) Mesotympanum. (3) Hypotympanum. (4) Area of resorption. (5) Incus. (6) Stapes. (7) Cochlea.

probably explains the frequent occurrence of otitis media in the children of one family as contrasted with the total absence of aural disease in other familial units; for persistent mesenchyme means inadequate ventilation and inadequate drainage and susceptibility to tympanal infection. Subclinical tympanal infection is much more common in childhood than is recognized, for the low grade middle ear

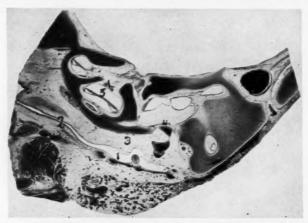


Fig. 5. Tympanum and Eustachian tube of a 3½ months fetus showing, as yet, very little resorption of mesenchyme (T. H. Bast collection). (1) Tympanum. (2) Eustachian tube. (3) Mesenchyme. (4) Footplate of stapes. (5) Cochlea.

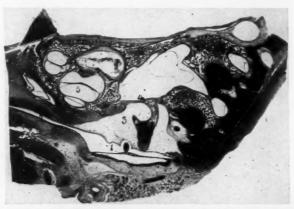


Fig. 6. Tympanum and Eustachian tube of a five months and three weeks fetus showing a large mass of mesenchyme completely surrounding stapes. Resorption of mesenchyme is well under way (T. H. Bast collection). (1) Tympanum. (2) Eustachian tube. (3) Mesenchyme. (4) Footplate of stapes. (5) Cochlea.

infections, complicating colds, may cause no other symptom than stuffiness and, therefore, escape detection. In an ear

free of mesenchyme the scant exudate in these conditions drains readily through the Eustachian tube and resolution occurs. Where drainage is not free, permanent changes occur (differentiation of mesenchyme into connective tissue). The

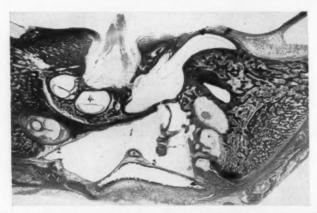


Fig. 7. Tympanum of an eight months fetus showing almost complete resorption of mesenchymal tissue (T. H. Bast collection). (1) Tympanum. (2) Mesenchyme. (3) Drum membrane. (4) Cochlea.



Fig. 8. Tympanum of a nine months fetus showing thin, normal mucosa. Complete resorption of mesenchyme (T. H. Bast collection). (1) Tympanum. (2) Mucosa. (3) Footplate of stapes. (4) Malleus. (5) Cochlea.

adhesive process occurring in the absence of history of otitis media, the so-called nonsuppurative or catarrhal adhesive process, is the result of such a change. Such children are also susceptible to purulent otitis media which readily transforms

tympanal mesenchyme into connective tissue. Such cases are apt to end with impaired hearing, whereas suppurative otitis media in a free tympanum usually undergoes perfect resolution, and hearing returns to normal.

In 1936, at the New York Postgraduate Hospital, I was privileged, through the courtesy of Marvin Jones, to study



Fig. 9. Masses of unresorbed mesenchyme in tympanum and filling additus. Acute suppurative otitis media (Marvin Jones collection). (1) Mesenchyme. (2) Tympanum. (3) Additus. (4) Pus.

the serially sectioned temporal bones of children who had died of aural infection and its complications. I was impressed by the presence of unresorbed tympanal mesenchyme in many of the specimens. Throughout the tympanic cavities were collections of pus pockets walled off by this embryonic tissue (see Figs. 9-14). The mesenchyme itself showed marked infiltration with inflammatory cells.

A tympanic infection can drain adequately through a myringotomy incision and Eustachian tube when mesenchymal masses are not present; but when this tissue persists, adequate drainage may be impossible, and the results are vascular invasion, periosteal necrosis, etc. In those cases where resolution finally occurs, there results a chronic adhesive process; for infiltrated mesenchyme readily differentiates into connective tissue.

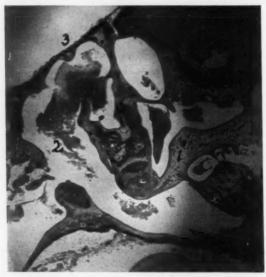


Fig. 10. Unresorbed mesenchyme in oval window niche with pus pockets. Acute suppurative otitis media (Marvin Jones collection). (1) Mesenchyme. (2) Pus. (3) Footplate of stapes.

The conversion of mesenchymal tissue into adult fibrous tissue is a most important factor in producing hearing impairment. Even in the absence of frank suppuration, this syncytium of stellate embryonal cells, as a result of any irritation, may differentiate into fibroblasts and then connective tissue. The irritation is abundantly supplied by recurrent upper respiratory infection and the subclinical tympanic reactions accompanying them.

Normally at the third fetal month, resorption of tubotympanal mesenchyme is initiated by ontogenetic biochemical

factors. By the eighth fetal month little is left, and at term we should find no trace; the lining membrane of the tympanum being almost as thin as in adult life.

Unfortunately, those ontogenetic biochemic factors which stimulate resorption of mesenchyme seem often to be deficient or are antagonized by other factors (probably hereditary), so that varying amounts of the embryonal tissue remain at term and may persist over a number of years.

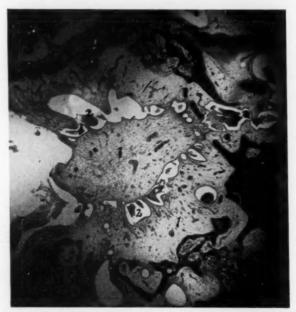


Fig. 11. Mastoid antrum filled with unresorbed mesenchyme. Numerous pus pockets. Acute suppurative otitis media (Marvin Jones collection), (1) Mesenchyme. (2) Pus pockets.

There is no doubt in my mind that the mesenchymal factor is of the greatest importance in determining ear disease or its absence. The child with an abundance of this tissue, through lack of adequate tympanal ventilation, is more susceptible to ear infection, and when infection occurs, it is more prone to chronicity and complications because of pus pocketing and impaired drainage.

There is dire need for recognition of this factor and for extensive experimentation. If we were able to detect in infants the presence of tympanal mesenchyme and if we had a method of producing its resorption at this early period, we would be far down the road of deafness prevention.

In 1936, Moses Lurie, of Harvard, told me of a strain of rats born deaf. Histologic study revealed unusual amounts

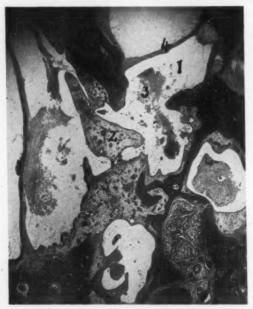


Fig. 12. Unresorbed mesenchyme blocking round window niche and forming a pus pocket in contact with secondary tympanic membrane. Acute suppurative otitis media (Marvin Jones collection). (1) Round window niche. (2) Mesenchyme. (3) Pus. (4) Secondary tympanic membrane.

of tympanal mesenchyme. Some of the rats, injected with anterior pituitary extract, regained their hearing and upon sectioning showed marked diminution in the amount of embryonal tissue.

Stimulated by this report, I carried out a similar research at the Veterans Hospital in Sawtelle but was unable to influence mesenchyme in young rats with anterior pituitary extract.



Fig. 13. Round window niche filled with infiltrated mesenchyme. Acute otitis media, suppurative (Marvin Jones collection). (1) Round window niche. (2) Mesenchyme. (3) Pus. (4) Cochlea.

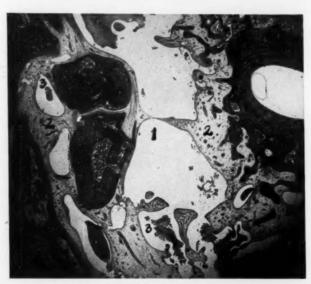


Fig. 14. Epitympanum showing unresorbed mesenchyme and pus pockets. Acute suppurative otitis media (Marvin Jones collection). (1) Epitympanum. (2) Mesenchyme. (3) Pus pockets.

The clinical results of tubal dilatation with the Gerjoye olive make me feel that initiation of resorption of tubotympanal mesenchyme is accomplished with the procedure. It is hoped that this paper may stimulate others to research along the same lines. Animal material offers ample opportunity for



Fig. 15. Mass of mesenchyme almost filling tympanum of immature rat. (1) Mesenchyme. (2) Tympanum. (3) Cochlea. (4) Cartilaginous capsule of labyrinth.

experimentation (see Fig. 15). Radium, X-ray endocrine extracts and various chemicals should be tried. Also, careful histologic investigations with this factor in mind should be made of children's temporal bones, particularly those with a history of otitis media and its complications.

#### DIRECT ADENOIDECTOMY WITH TUBAL DILATATION.

Although this procedure has already been reported, it seems best to repeat here the various steps of the operation. Ether anesthesia is used. Where tonsils are to be removed they should be enucleated before the adenoidectomy. After all bleeding has been controlled the soft palate is gently elevated with the Andy Love retractor. A complete view of the entire nasopharynx is obtained. If the tubal orifices are visible, dilatation should precede the removal of lymphoid tissue. The tubal orifices present as slits or dimples; an entirely different picture from that obtained with the nasopharyngoscope or mirror. The Gerjoye dilator is inserted into the right Eustachian tube; pressure being exerted for 25 seconds, and then repeated on the left side.

Next, with the soft palate elevated, the central mass of lymphoid tissue is removed with the smallest La Force adenotome. Bleeding is controlled with gauze tampons moistened with adrenalin chloride. Lateral adenoid, around and covering the tubes, is then removed with my triangular forceps and curved scissors or with a nasal biting forceps. In lifting the adenoid with the triangular forceps care must be exercised not to include mucous membrane. The final step is to remove the lateral curtains. These are lymphoid masses posterior to the posterior pillars of the fauces. The punch forcep presented in my original paper has been discarded as not entirely satisfactory. I now grasp the lateral curtain with the triangular forcep and remove it with the curved scissors.

No after-treatment other than that routinely employed after tonsillectomy and adenoidectomy is indicated. The first audiometry is usually done within three weeks.

We have had but few recurrences since employing the direct method, and most of these have been in allergic children. It would seem that the great number of adenoid recurrences reported, for the most part, have been incomplete operations; incomplete because done blindly.

It is hoped that intravenous or rectal anesthesia with the removal of lymphoid tissue by means of electrocoagulation will soon be possible. Electrocoagulation would be used only where a previous adenoidectomy had been performed and relatively small amounts of lymphoid tissue remain. It would

not displace the La Force adenotome where a large adenoid presents.

Tubal dilatation has been tried in adults but without any success.

One point is of the greatest importance: One should be sure that he sees plainly the tubal orifices before inserting the Gerjoye dilator. It would not be safe to trust the sense of touch in locating these openings.

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1033 Gayley Avenue.

#### MENIERE'S SYNDROME.\*

Dr. J. Hallock Moore (by invitation), Huntington, W. Va.

Since 1861, when Ménière¹ described a disease entity which bears his name, there has been much controversy over the physiopathological mechanism which produces this symptom complex. In my estimation the condition is more of a physiological nature with probably only a very slight and transient pathology; therefore, it falls into the category of a syndrome rather than in that of a disease. Dandy² and others divide the syndrome into two types: The true syndrome complex and a pseudo-variety. I disagree with this arbitrary division and feel that the two conditions are the same entity and only differentiated by the degree of the symptoms. Furstenberg² and other observers agree in this contention.

The literature has been reviewed by Johnson, Brunners and Weiss, and by practically all other investigators of recent years, so I shall only briefly outline the methods and results of their labors.

Mygind and Dederling<sup>7</sup> felt that due to a faulty water metabolism there was a retention of fluid in the labyrinth which resulted in the aural symptoms. By instituting a low sodium diet, hospitalization for two weeks and inflating the ears they cleared up many cases.

Furstenberg<sup>3,8</sup> thought that the above observers obtained their results by the elimination of an electrolyte, — sodium. Thus, by restricting the amount of sodium chloride in the diet and increasing its elimination by the administration of ammonium chloride, he has helped others.

Talbot and Brown recognized that Furstenberg's diet had a high potassium content. As symptoms could not be reproduced by hydration, alkalosis or increased sodium concentration, they discarded the sodium ion hypothesis and prescribed large doses of potassium chloride. They suggest that the proper conduction of the nerve impulse is found when there is an optimum concentration of potassium.

<sup>\*</sup>Read by invitation at the meeting of the Southern Section, American Laryngological, Rhinological and Otological Society, Chattanooga, Tenn., Jan. 28. 1943.

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Harris and Moore<sup>10</sup> advocate a high protein diet plus nicotinic acid and thiamine chloride. They use inflation locally.

Atkinson<sup>11,12,13</sup> divides Ménière's syndrome into two groups from an etiological standpoint. The mechanisms are vasopastic and allergic. These may be differentiated by the histamine skin test. He infers that the pathology is probably a cloudy swelling in the labryinth and that many patients can be aided by inflation of the Eustachian tubes. He points out that thiamine chloride is a cholinergic and some of its results are due to its vasodilatation. He later advocates the use of a less drastic vasodilator than histamine.

Shelden<sup>14</sup> and Horton<sup>15</sup> advance the hypotheses that the most likely factor in the production of the syndrome is a local alteration in the permeability of the capillary wall, resulting in local edema. Histamine is an important agent which affects capillary permeability; therefore, histamine should relieve the local congestion and benefit the patient. In many cases this has proved to be true. They also report two types of tinnitus: One, high pitched, which is neurogenic, and the other low pitched and synchronous with the heart beat, which is vascular.

Tobey<sup>16</sup> apparently feels that there are many etiological factors in the production of the syndrome, for he states that systemic disease, endocrine disorders, avitaminosis, allergy, toxic dehydration and Eustachian salpingitis must be ruled out before trying the other methods of therapy outlined above.

All of the above authors report failures and practically all advise surgery in intractable cases. Dandy<sup>2</sup> strongly urges this. Walsh and Adson<sup>17</sup> feel that if medical means fail, surgery is indicated and is the most certain cure. Walsh advocates potassium nitrate in large doses instead of potassium chloride. Crutchfield<sup>18</sup> feels that medical measures should be given an adequate trial before surgery is utilized.

From the above array of literature the consensus of opinion is that the condition arises within the inner ear. The majority of investigators lean toward the hypothesis that there are pressure changes within the labyrinth due to varying causes, which bring on the syndrome. Shambaugh<sup>19</sup> stated that upon accidentally opening the epithelial sac in the

horizontal canal during a fenestra ovalis operation for deafness, the perilymph was under practically no pressure, as only one drop exuded from the opening.

Some work has been performed on pressure changes in the middle ear, but first let us review the physiology of the Eustachian tube. Rich<sup>20</sup> proves that the Eustachian tube does not open from an inequality of pressure upon the two sides of the tympanic membrane. The tube opens only during deglutition, sneezing and vawning. Stimulation of the tensor palatii caused a wide gaping of the Eustachian orifice. It has long been a recognized fact that an inequality in pressure upon the two sides of the tympanic membrane causes a serous secretion within the middle ear, and a hyperemia of the drumhead. This occurs in every case of otitis media catarrhalis acuta. The hyperemia undoubtedly extends to all of the lining mucosa of the middle ear, and must also involve the labyrinth which is separated only by the membranes in the round and oval windows and the thin bony wall. Besides the above, the ossicular chain pushes the stapes into the oval window, increasing the pressure in the labyrinth. Van Dishoeck<sup>21</sup> has shown that the hearing is best when the pressure within the middle ear is equal to that in the external canal. This was accomplished by means of the pneumophone which delivers a constant low tone to the ear via a rubber tube while the pressure on the tympanum is lowered from positive to negative. Tension on the drum muffles sound and under greater positive or negative pressure the ossicular chain plays a part. We have all experienced the same effect upon ascending or descending from a given altitude. Loch22 proves that by blocking the Eustachian tubes in man for one and one-half hours there is a loss of the high tones.

In chronic catarrhal otitis media the Eustachian tubes may be blocked either partially or completely for years. In this condition, is it illogical to assume that there is a low grade hyperemia of the lining mucosa of the middle ear, especially when upon inflating such an ear it is frequently found filled with serum which can be seen through the tympanic membrane? Hence, is it unreasonable to suppose that in the presence of a long standing hyperemia in the middle ear it would not extend to the labyrinth and cause pressure changes either of a vasomotor or hydropic type?

This would result in a cloudy swelling of the membranous labyrinth, which many of the aforementioned investigators suggest and which Hallpike's<sup>23</sup> autopsies tend to confirm. It would also explain the lack of pathology found at postmortem. Furthermore, it gives a logical reason for the success of the various treatments outlined in the literature.

In many allergic patients, those with a rhinosinusitis, those with endocrine dyscrasia, those with a mechanical obstruction of the nasopharynx, there is found a stoppage of the Eustachian tubes. This may have been present for years without the patient suspecting it until either pain, tinnitis, deafness or vertigo called it to his attention. I have had patients tell me that they did not realize how stuffy their ears were until I had relieved them. This does not occur in young children because their Eustachian tubes are shorter and more active than in later life. Adenoids can cause an obstruction, but I question if this is constantly present. In the presence of deafness due to adenoids the history is usually one of improvement in hearing at times, but it becomes worse when the child has a cold.

With this in mind it is easy to see why a low sodium intake could benefit the condition, as it would tend to lessen water retention throughout the entire body and must of necessity lessen any local aural edema. The ingestion of large amounts of the potassium and ammonium salts acts in the same way; therefore, the pressure in the labyrinth would be lowered and the vertigo lessened.

The value of histamine in the treatment of Ménière's disease lies chiefly in the group of patients that is allergic. Histamine can control many asthmatics and hay fever patients by its detoxifying effects. This is true of the vasoconstrictors as well. Vaughan<sup>24</sup> points out that skin tests are unreliable in their presence, and this applies to histamine. Is it incorrect to attribute the success of the histamine therapy in Ménière's syndrome to its antiallergic properties which would tend to lessen the vasomotor rhinitis and the edema of the Eustachian tube, the middle ear and the labyrinth?

As to thiamine chloride and nicotinic acid, Atkinson<sup>11</sup> points out that the former is a cholinergic and that this action may be responsible for some of its benefit.

Many investigators utilize inflation as an adjunct to their other modes of therapy, and I wonder if some of their successes cannot be attributed to the adjunct rather than to the therapy itself.

In an analysis of 20 cases I found the following symptoms: Nineteen cases upon careful questioning gave the history of an aura of from six months to several years' duration prior to the onset of vertigo. This consisted of a slight stuffy sensation in the ears. Several of these patients had consulted me a year or more previous to their first vertiginous seizure, and in a routine examination I found retracted tympanic membranes. After inflating the Eustachian tubes, these patients admitted that their ears had felt stuffy. The onset of this had been so gradual that they did not realize that the condition existed.

Six of the patients stated that they had no tinnitus. It was present in all the others. Nine had a definite horizontal nystagmus. Eleven were without this symptom but were not seen during an acute seizure. All 20 had definite vertigo of varying degrees of severity. This was accompanied by nausea in 14 cases and was severe enough to cause vomiting in nine.

Fourteen were unable to work, and deafness of varied degree was present in all but two cases. Audiograms taken showed various types of deafness.

The age of the group ran from 25 to 81 years, the bulk being in the third and fourth decades. Fourteen were females. Nine had unilateral ear involvement, but even in this group the other ear did not inflate quite normally. Six patients were seen in their first attack; the others had had two or more seizures. Some had been treated by other methods without result.

Seventeen had nasal sinus disease. Three had endocrine dyscrasies. Four were allergic. Two had nasal obstruction due to septum deviations. One gave a history of a mastoidectomy 16 years ago. Ten patients complained of pain or discomfort which was referred to the affected ear in five, to the vertex in two, and to the occiput in three. In several instances the discomfort would involve several of these areas simultaneously, such as the ear and vertex, etc.

In the treatment of these cases I have adhered to vigorous, thorough inflations and bouginage of the Eustachian

tubes, and in practically every case the vertiginous seizure has been relieved. The allergic patients have been placed in the hands of competent allergists, and after once the Eustachan tubes have been thoroughly opened, occasional inflations have maintained this status and prevented recurrence of the syndrome. Of course, all nasal pathology has to be cleaned up, and endocrine disorders handled by the internist. Many of these patients return for inflation upon the slightest sensation of stuffiness in their ears, and 14 of them have been kept free from vertigo for several years. Two cases have had the VIIIth nerve severed. One had a recurrence of vertigo, at which time the other ear was found to be involved, and a few inflations restored her equilibrium. Incidentally, an inflation of the operated ear found it full of serum, and the patient was much relieved from a sense of pressure after its removal.

By inflation I mean catheterization of the Eustachian tube and air introduced by means of the Dench bag. In one case the ear was apparently open, but after a bougie was passed an entirely different sound was heard in the middle ear, and the patient was immediately relieved. If there is any doubt in the operator's mind as to the status of the patency of the tube, I advocate passing a bougie. It may be said that these results are spontaneous remissions, but I have seen these patients relieved right in my treatment chair too frequently to even tolerate the idea.

As to the number of inflations needed to bring about complete relief, it varies with each case. Sometimes one will suffice, but usually it requires four or more, and the patient shows a gradual improvement between treatments.

Some of the above cases are of sufficient interest for a more detailed account:

One patient, a cardiac, age 55, I saw in consultation over two years previous to her first attack of vertigo. In my routine examination I noticed that her tympanic membranes were retracted. Upon asking her if her ears did not feel stuffy she replied, "Yes, slightly." I inflated them on the succeeding day with relief. Two years later I was called to her home. She was lying in one position in bed, and had been unable to keep anything in her stomach for two days. She had a constant horizontal nystagmus with the quick component to the right. The left eardrum was found to be retracted. After a bilateral inflation, the nystagmus and nausea disappeared immediately. Her sister called me that night and said that she was better but afraid to move for fear of starting another attack. I reassured her and three days later when I returned she was sitting up in a chair. No nystagmus was present, and she had not vomited since the inflation, I reinflated both ears. She was to call

at my office in four days, but called me and said her ears were open and that she felt fine. I advised her to phone me if her ears felt stuffy. To date I have neither seen nor heard from her, but through a colleague I know that she has had no return of her symptoms.

Another case, a white male, school teacher, age 33 years, was practically carried into my office. He had been diagnosed by a local general practitioner as having a brain tumor. For two weeks he had been unable to walk or retain any food in his stomach. He stated that he had always had a roaring in his head. Inflation and bouginage gave some relief, after 10 inflations his vertigo was entirely gone, the tinnitus cleared up completely, and an audiogram showed a normal hearing curve. This was 14 months ago and he has had no recurrence.

A case which is under my care at present is a white male, age 33. He is a railroad mail clerk who in the last three months has been unable to make but nine runs because of vertigo, nausea and vomiting. He had been to a well known clinic, but even though he had faithfully followed their outline of treatment had received little or no benefit. He had been deferred twice from a civil service examination because he had been unable to concentrate. The two weeks prior to his first visit to my office he had been unable to retain anything in his stomach.

He was reeling when he came into the office and showed a definite horizontal nystagmus with the quick component to the right. After an inflation the nystagmus stopped, and he walked steadily out of the office, ate and retained a large meal. Two days later he returned. At this time he said he was only slightly nauseated but had a tendency to walk to the left. He was reinflated and again all his symptoms disappeared. Two days later he was again inflated and was able to work 140 hours in the next 11 days, with one day off between trips. Unfortunately, he caught a severe cold on his last trip, which caused a left maxillary sinusitis. This renewed his symptoms, which again responded to irrigations of the antrum, plus inflation and bouginage. I saw him several days ago, and he has had no return of his vertigo and states that he is now working on his civil service examination, a thing which had been impossible for the past three months.

The three above cases illustrate the management of the others, and where the patients have co-operated, I have been able to relieve their vertigo by persisting with the inflations.

In closing, I have brought little that is new to you in this paper. From 20 cases no conclusions should be drawn; however, I feel as do the majority of investigators of Ménière's syndrome that it is caused by pressure changes in the labyrinth, and I suggest a hypothetical mechanism to explain the physiopathology. Before going into the fields of biochemistry I feel much as Atkinson does, that a few vigorous inflations plus bouginage should be attempted, and in many cases the results will be startling. It requires neither an elaborate laboratory nor costly apparatus.

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#### DISCUSSION.

Dr. John J. Shea (Memphis): I congratulate Dr. J. Hallock Moore upon his presentation. He is correct in his observation that many of the inflations now require catheterization of the Eustachian tube. But there are patients who are having Ménière's syndrome, the result of an intoxication from the poisons arising from the liver, gall bladder and colon, which have a selective action upon the labyrinth, and of these histamine is the most potent. We are constantly producing histamine in our intestinal tract and sensitivity to it is manifested by an increase of the fluid in the labyrinth. Histamine is a powerful physiological stimulant and when administered parenterally will increase the production of all the human secretions, including the cerebrospinal fluid.

The treatment we have found most satisfactory consists in the administration of an initial cathartic (calomel gr. 3, sodium bicarbonate gr. 10, followed by epsom salts oz. 1 in four hours), and the desensitization by the administration subcutaneously of histamine acid phosphate. patients who are sensitive to histamine as demonstrated by a cutaneous reaction or the re-establishing of headache or vertigo are desensitized by increasing doses starting with one-fourth cc. of a concentration consisting of a concentrate of 2.75 mg. in 5 cc. As soon as the patient can tolerate one-half cc. twice a week, this maintenance dose is continued until you are satisfied that the patient has been relieved and re-establishing upon the return of the symptoms to supplement the desensitizing process. A tablet of torantil (10 units, histamine) is given after the two principal meals to serve as a ferment and to split the histamine constantly existing in the intestinal tract. A cholagogue of the following: Tr. Belladonna 10, Tr. Cardamon Comp 10, Sodium Bromide 10, Cascara Evac. 10, Diazyme 30, Chologestin 180, two teaspoonfuls are administered in water each night to reduce the toxic action of the hepatic by-products. The duration of the treatment is uncertain. In some instances a month will be sufficient to give relief from the vertigo or headache.

If at any time the vertigo becomes severe, an intravenous dose of histamine 1 mg., diluted in 250 cc. of normal saline and administered at the rate of a drop per second, will relieve immediately the majority of symptoms. Lately prostigmine has been advised as a substitute or when the histamine fails. Various methods of administration have been suggested, the later being—a 15 mg. tablet of prostigmine is dissolved in 30 cc. of water and the resulting solution is administered as follows: On the first day, one, two and three drops are given morning, noon and night, respectively. The increase of one drop per dose is maintained until 30 drops are reached, following which 30 drops are given each day for one week and then three times per week for an indefinite period. Occasionally, when it is felt that the results could be improved, the dose is increased to 40 drops. (The Treatment of Severe Periodic Headaches with "Desensitizing" Doses of Prostigmine. Louis Pelner and M. E. Aibel—Current Medical Digest, pp. 39-42, Dec., 1942.)

# OTOSCLEROTIC FOCUS OUTSIDE THE INNER EAR CAPSULE.\*

DR. GEORGE KELEMEN, Boston.

Reports on pathological findings similar to otosclerotic foci elsewhere than in the inner ear capsule are exceedingly rare. Katz. in 1906, described a case of otosclerosis in a cat; the head of the malleus and the body of the incus showed deeply stained areas in the center of which Haversian canals or marrow spaces could be recognized: these areas consisted of newly formed and subsequently sclerosed bone such as is seen in otosclerotic foci. Ruttin,7 in 1933, found in exostoses of the external auditory canal a dense fibrous tissue rich in cells. which contained oblong ramifying bone lamellae. In their center there was a nucleus of dark reticular bone, surrounded by a wide osteoid margin; the bone itself consisted mainly of residual lamellae, and these in their disorder reminded one of old otosclerotic bone; the intercellular substance formed everywhere clearly marked lines. Kelemen. in 1939, described in an operatively removed osteoma of the frontal sinus in the vicinity of the lamina interna of the frontal bone, a small area of breccia-formation, reminding one of old otosclerotic bone. Examination under polarized light revealed how the lamellary structure disappeared more and more and how the bone formed from fibrous connective tissue assumed increasing complexity; sharp blue boundary lines made the resemblance to an otosclerotic focus still more conspicuous. Covell.<sup>2</sup> in 1940, found typical otosclerotic foci in the malleus and incus of both temporal bones of one individual. In a large percentage of other material handled by him, he noted alterations in the ossicles bearing a certain resemblance to the so-called blue mantles of otosclerosis.

There are some reports of osteoporosis in connection with otosclerosis. Bryant, in 1908, described vascular osteitis, osteoporosis and hyperostoses of the ossicles together with typical otosclerosis. Fraser and Muir, in 1916, found a case

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<sup>\*</sup>From the Department of Otolaryngology, Tufts College Medical School, and the Mosher Laboratory of the Massachusetts Eye and Ear Infirmary; aided by a grant from the Charlton Fund.

with several foci in the areas of predilection; the bony walls of the attic cavity showed marked osteoporosis and stained deeply with basic stains. Fig. 10 of their publication shows "spongification of bone in the wall of the mastoid antrum."

Jones, in 1941, discussed cases with otosclerotic foci in the inner ear but outside the region of the cochlea and oval window.

The following histological observation may be of interest in connection with the above reported findings.

The temporal bones of a 14-year-old boy, who died after osteomyelitis of the frontal bone which produced a collateral subacute otitis (case to be reported in detail), were sectioned in the horizontal plane and stained with hematoxylin and eosin. A high degree of pneumatization was present; no otosclerotic changes could be noted. In the pneumatic cells of the right tegmen tympani, one of the intercellular osseour partitions showed a peculiar structure. This area was very conspicuous amidst the surroundings which did not deviate from the usual anatomical structure. The range of serial sections showing this formation could be followed through a depth of about 300 micra, beginning almost immediately below the cortex of the tegmen. This particular partition which was sharply limited from the adjoining cellular walls consisted of a reticulized bone of honeycomb appearance. Onehalf of it protruded into the lumen of one of the surrounding cells in shape of a tumor-like growth.

The outstanding microscopical feature of this area was the change that had taken place in the lamellary system with division of the units of the latter into short trabeculae of different size and shape. The marrow spaces were much wider here than anywhere else in the surrounding tissue. The vessels were imbedded in a loose connective tissue rich in cells: they were numerous and conglomerate but without evidence of hyperemia. One surface of this reticulated bone was smooth, where it was adjacent to the lumen of one of the adjoining pneumatic cells, with vascular channels and small marrow spaces opening directly underneath the mucoperiosteum. The other surface was equally smooth for one-half of the length of the wall while the other half was elevated in shape of a bony growth, drawn out into a sharp point. Within the area of this outgrowth, appearing in the sections in the

shape of a triangle, a different kind of bone was noted. The staining was distinctly darker; the marrow spaces were much smaller, barely giving space to a single vessel; there were no rows of osteoblasts. The trabeculae of the bone were much smaller, with ragged edges and some ground substance between them; there was no definite system in their disposition; the general aspect was one of debris. Yet the bone cells in this area were as well stained as those in the larger, spongy part. The covering mucous membrane was everywhere thickened, corresponding to the condition of inflammation prevailing in this temporal bone; however, it was compressed and

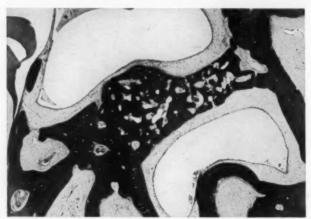


Fig. 1. Isolated focus amidst the normal osseous framework of the tegmen. Spongification with enlarged and richly vascularized marrow spaces. X20

reduced to a very thin layer at the tip of the tumor-like projection.

Comment: This peculiar formation, suspended in the intercellular walls of the pneumatized tegmen, corresponds in its larger part to the spongification of the bony framework in otosclerosis, at a stage when attempts at condensation are once more apparent, as represented by intensive osteoblastic activity. The small projection shows a typical "breccia," a detritus formed by the remnants of trabeculae. The structure tends to disappear here, thereby producing a picture of increased complexity. The vascularized spongy part corresponds to a progressive stage while the breccia formation

may be considered, as in other pathological bone conditions, as the end-stage of the process. Blue mantles around vessels are missing, but sharp lines formed by scarce intercellular substance can be distinguished between the trabeculae of the detritus.

The part of the cartilaginous ear capsule forming the roof of the tympanic cavity ossifies around the so-called pterotic ossification center. Irregularities of development produce here dehiscences but no cartilaginous remnants were reported in this region with its rapid changes of bony structure in the course of the process of pneumatization. In this way the pres-

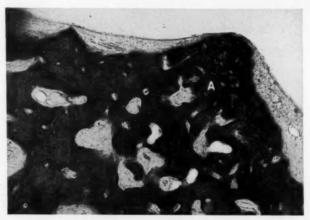


Fig. 2. Tip of tumor-like outgrowth, showing at "A" condensation with maximal reduction of the marrow and vascular spaces and dissolution of the trabeculae into a debris, a breccia. X400.

ence of this focus hardly could be brought in connection with pre-existing cartilage. The spongiotic part of the structure reminds one of osteitis fibrosa, in the stage of new bone formation by rows of osteoblasts, while the breccia-like part offers analogies with the mosaic appearance of bone in Paget's disease. Similarities between the two conditions and otosclerosis have been stressed often. But no signs of osteitis fibrosa or osteitis deformans were present in the patient's history and it would be equally unjustifiable to presume a connection between the acute osteomyelitis and the formation of this focus.

The origin of an otosclerosis-like focus at this location is as unclear as is the origin of the foci in the areas of predilection. This finding would indicate that the conditions which have to prevail in order to produce an otosclerotic focus may not be entirely restricted to the inner ear capsule.

Summary: Histological description is given of a single unilateral focus similar to the product of otosclerosis, forming the wall between two pneumatic cells in the immediate vicinity of the cortex of the tegmen antri. The contribution seems to be justified by the extreme infrequency of findings similar to otosclerotic changes outside the bony inner ear capsule.

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414 Beacon Street.

# A NEW SULFA COMPOUND, DESOXYEPHEDRONIUM SULFATHIAZOLE, FOR THE TREATMENT OF SINUSITIS.

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A new group of sulfa compounds was discovered as a result of work on stabilization of aqueous solutions of salts of the sulfa drugs, and incorporation of vasoconstrictors.

For example, in a stable solution the sodium salt of sulfathiazole combines with d1-Desoxyephedrine hydrochloride to form Desoxyephedronium Sulfathiazole.

A report on the chemistry of these new compounds is in preparation for publication.\* The twofold purpose of this paper is to introduce Desoxyephedronium Sulfathiazole -C19H24N4S2O2 - and, more especially to present the clinical aspects of a 2.5 per cent stabilized aqueous sodium sulfathiazole with 0.125 per cent of d1-Desoxyephedrine hydrochloride, hereinafter termed D. O. E. Sulfa for brevity.

Fig. 1. Desoxyephedronium Sulfathiazole.

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<sup>\*</sup>Jour. A. C. S.; in publication, 1943.

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In a previous publication Turnbull<sup>1</sup> pointed out that solutions of sodium sulfathiazole were effective in treating infections of the eye, ear, nose and throat. These solutions were unstable and became discolored and irritating.

Two general types of changes were found to affect the unstable solution; the first usually occurs upon contact with air, the second usually results from exposure to light. The types of reactions encountered may be exemplified by the following chemical expressions:

1. In air the outstanding reaction probably is:

(Soluble Sodium Sulfathiazole)

(Relatively Insoluble Sulfathiazole Crystals)

But some slight oxidation may also occur while precipitation is taking place.

2. In light the main change appears to affect only a small portion of the drug, and it may be indicated as:

(Soluble Sodium Sulfathiazole)

(Soluble Sodium Salt of Nitroso Derivative, Highly Colored)

But the oxidation reaction is complex and only one of the many possibilities is shown.

Studies undertaken to prevent this deterioration resulted in the following formulation:

#### STABILIZED SODIUM SULFATHIAZOLE WITH d1-DESOXYEPHEDRINE HYDROCHLORIDE (D. O. E. SULFA):

Sodium Sulfathiazole	2.5 2.0 1.0 0.125	per cent per cent per cent per cent
Flavor solution Color solution Adjusted to pH of approximately 8.6. Sterilized by autoclave.	0.220	por conv

Histological sections from rabbits treated for 10 days, three times a day, with sulfite-stabilized 2.5 per cent solution of sodium sulfathiazole with 0.125 per cent of d1-Desoxyephedrine hydrochloride.



Fig. 4. Section through the air-filtering mechanism-magnification 160X.

D. O. E. Sulfa is practically unaffected by light, air, oxygen and heat.

Stabilization made possible permanent incorporation of a vasoconstrictor in the solution. Various vasoconstrictors were tried and d1-Desoxyephedrine hydrochloride was found to be compatible and clinically effective.

# d1-desoxyephedrine.

d1-Desoxyephedrine was first prepared by Ogata<sup>2</sup> in 1919, but it attracted little interest until about 20 years later when

several articles appeared, chiefly in German medical journals, reporting that it acted like amphetamine in producing central stimulation, but unlike amphetamine, it did this without causing undesirable reactions. Clinically it has been widely used in Germany for its effect in elevating the mood, decreasing the sense of fatigue and counteracting sleepiness. It has a vaso-constrictor action on the nasal mucosa similar to that of ephedrine.

Through the courtesy of Dr. E. H. Volwiler, of Abbott Laboratories, a supply of d1-Desoxyephedrine hydrochloride was

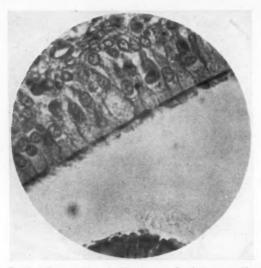


Fig. 5. Section through the air-filtering mechanism-magnification 670X.

obtained. It was noted that effective vasoconstriction produced by the combination of one-eighth of 1 per cent of d1-Desoxyephedrine hydrochloride with the sodium sulfathiazole was comparable to that expected with approximately 1 per cent aqueous d1-Desoxyephedrine hydrochloride alone.

The explanation of the marked increase in activity of the vasoconstrictor when combined with the stabilized sodium sulfathiazole was pointed out to us by Chen<sup>3</sup> as a synergism. We later corroborated this synergistic action by manometer readings following the technique of Sternstein.<sup>4</sup>

The synergism permitted the use of a very small proportion of the vasoconstrictor, thus overcoming the possible occurrence of side-effects usually experienced when a patient uses an ephedrine compound frequently over a long period.

Incorporation of this vasoconstrictor, therefore, appeared to give the optimum clinical result — that of shrinking swollen tissues and at the same time promoting drainage and ventilation of the sinuses without the after-effects so commonly experienced with use of the usual vasoconstrictors; after-effects such as congestion of the membrane, sneezing, tachycardia and nervousness.

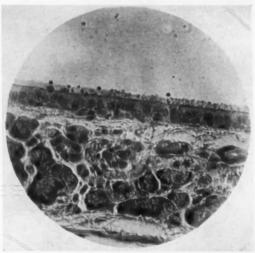


Fig. 6. Section through the posterior junction area—magnification 400X. Note freedom from cellular infiltration and intactness of the epithelial layer.

Addition of the stabilizer and incorporation of the vasoconstrictor permitted reduction of the strength of the sodium sulfathiazole from 5 to 2.5 per cent.

When D. O. E. Sulfa was used in packs in the nose on acutely swollen membranes and left in place for 20 to 30 minutes relief was noticeable, and patients reported improvement the day following treatment, instead of the usual complaints after former methods of treatment, with comments of "no relief" or "worse, with a sleepless night."

#### ALKALINITY.

Comparative study of nose drop medications shows widely varying pH\*:

Compound	рН
1% Neosynephrin (Stearns)	2.5 - 4
Isophren Solution (Brommel)	-2.5 - 4
1% Propadrine (Sharp & Dohme)	3.8 - 5
3% Ephedrine Solution (Lilly) (Single sample)	3.9
Gluco-Fedrin (Parke, Davis)	4.8 - 5.8
Isedrin Compound (1% Ephedrine Sulphate) (Lilly)	
(Single sample)	6.0
5% Solution Argyrol (Single sample)	8.9 - 9.1
Metaphedrin Aqueous Isotonic (Abbott) (Single sample)	10.0
1% Ephedrine Compound in Oil (Lilly) (Single sample)	10.0

<sup>\*</sup>Values given are subject to changes dependent upon the age and condition of the preparations.

# The pH of D. O. E. Sulfa is 8.6 — 9.

# IS DH IMPORTANT?

The first work on ciliary motility was done by Todd in 1835. Since then there have been numerous observers. The recent work of Negus, of England, deserves wider dissemination in this country. Negus shows that if the pH of the nasal medium is lowered to 6.4 or less, ciliary action cannot continue; the paralytic effect is very obvious as compared with the maintenance of vigorous action for 24 hours or more in a physiological saline solution of pH 8.5.

Gray<sup>†</sup> found greatest activity of the cilia in Tyrode's physiological saline solution, pH 8.2 to 8.5.

Schafers found that a pH of 8.6 is the most favorable to ciliary motility.

Gray<sup>7</sup> showed the pH necessary to stop ciliary motility in one minute was as follows:

HCl, pH 3.4; citric acid, pH 3.4; acetic acid, pH 4.8; butyric acid, pH 5.2.

Negus<sup>e</sup> states: "It is well known that acid solutions paralyze cilia."

It has long been known that dilute alkaline solutions quicken ciliary activity. All workers except Fabricant have reported that the pH of normal nasal mucus is practically neutral — 6.5 to 7.5. Fabricant working in situ reported on the acid side — 5.5 to 6.5. He maintains that nose drops

should be acidic, whereas the work of Negus and numerous other observers shows that ciliary action is destroyed when the medium is acid.

Electrometric pH measurements in situ may be subject to the influence of variables such as:

- a. pH of the blood;
- b. pH of the skin;
- c. acidity due to variation of CO, in respiratory gases;
- d. electromotive forces of the body.

In order to overcome these variables we used Nitrazine pH indicator paper. The range of coloring gradation of Nitrazine test paper runs from about 4.5 to 7.5 pH. The sensitivity permits reading of the pH to within 0.5 pH or less. In 100 consecutive tests in situ in normal noses, acute and chronic infections, and allergy and polypoid membrane, the pH was neutral or alkaline in all cases, none being on the acid side.

## ANTIBACTERIAL ACTION OF THE SULFAS IN RELATION TO DH.

The antibacterial efficiency of sulfonamides as measured by their ability to overcome p-aminobenzoic acid has been shown to be dependent upon the pH of the medium.

For sulfonamide therapy it would appear that the pH of infected loci should be maintained at the highest physiologically acceptable value.<sup>10</sup>

As the active agent in sulfonamide therapy is an anionic species<sup>10</sup> and the solubilities and effectiveness of these drugs increase with alkalinity,<sup>11</sup> a solution of pH of 8 to 10 is indicated as being antibacteriologically desirable.

# SUMMARY ON ALKALINITY.

It has been concluded that a mildly alkaline sulfonamide solution is preferable for nasal medication because:

- 1. The sulfonamides have greatest bacterial action in the pH range 8 to 10.9
- 2. Ciliary motility is least affected by mildly alkaline solutions pH 8.5 and slows down in slightly acidic solutions, pH 6.5 or less. 10

- 3. D. O. E. Sulfa, mildly alkaline, allows ciliary activity to continue.
- 4. Secretions from nasal mucous membranes are normally slightly alkaline.
- 5. Effective concentrations of the sulfonamides are readily obtainable in mildly alkaline solutions.

#### EFFECT ON NASAL MEMBRANE OF RABBITS.

The effect of spraying rabbits' nasal membranes with the sulfite-stabilized solution of sodium sulfathiazole with d1-Desoxyephedrine hydrochloride has been studied thoroughly at The Squibb Institute for Medical Research.

"Spraying was accomplished by the use of a DeVilbiss atomizer, approximately 0.6 cc. being introduced into each nostril three times daily for a total of 30 treatments. The distribution of the material was determined by examining the stained areas of the nasal passages and sinuses 15 minutes after the animals had been sprayed, the solution having been stained with carbol gentian violet. As controls for the eight rabbits so sprayed, eight other rabbits were treated with saline and six were left untreated. All the animals were sacrificed on the last day of treatment and subjected to gross and microscopic examination. Throughout the test period the treated rabbits showed no nasal discharges or adverse respiratory effects. Gross examination of the nasal air passages and sinuses and of the trachea showed nothing abnormal in any of the rabbits. Sections were taken from four areas; an anterior area through the air-filtering mechanism, a middle area adjacent to the sinuses, a posterior area at the junction with the pharynx and through the trachea. Microscopically there was no significant difference between the appearance of the mucosa or submucosa of the nasal cavities or of the trachea of either the treated rabbits or of the controls. One rabbit treated with the product showed an acute low-grade localized infection confined to a few tips of the maxillary turbinate. However, one of the saline-treated and one of the untreated rabbits also showed such low-grade inflammatory reaction.

#### PHYSIOLOGICAL EFFECT.

"In the spraying tests it was observed that gentian violet could be found in the ethmoid turbinates and in the paranasal sinuses at 15 minutes but not at 30 minutes. This indicates that the product does not interfere with nasal secretion.

#### SYNERGISTIC VASOCONSTRICTOR EFFECT.

"In order to determine the local vasoconstrictor effect of the product, it was instilled into the eyes of rabbits, 0.5 cc. of solution being used for each rabbit in one eye, the opposing eye being used as the control, the treated eye being reversed on the following day. Rabbits were also treated with the vasoconstrictor alone, using strengths of 0.12 to 0.5 per cent. These tests showed that the local vasoconstrictor activity on rabbit conjunctiva of the product (which contains 0.125 per cent of the vasoconstrictor) is considerably greater than is that of a 0.125 per cent simple aqueous solution of the vasoconstrictor (11 per cent instead of 100 per

cent incidence of blanching). In fact, the blanching effect of the product was found to be approximately equivalent to that of a 0.5 per cent aqueous solution of the vasoconstrictor."

#### CILIARY MOTILITY.

An analysis of the effect on ciliary activity has been worked out in a comprehensive report by The Squibb Institute for Medical Research.

"For purpose of comparative determinations of the effect of solutions on ciliary motility, the ciliated mucosa of excised rabbit trachea are used as a test site. Portions of trachea are immersed in the test solutions and from time to time strips are cut from the mucosa and examined for ciliary activity. Under these nonphysiologic conditions the periods of ciliary motility are greatly reduced as compared to those observed with the reflecting microscope on exposed ciliated surfaces in the live animal where normal blood circulation and secretory function are operative. With proper control and expert technique the more practical excised trachea method does, however, yield valid data in respect to the relative activity of different preparations in their inhibiting action on ciliary motility and injury to cilia.

"In the experiments with the sulfite-stabilized solution of sodium sulfathiazole with d1-Desoxyephedrine hydrochloride, the rabbits were killed by spinal section or air embolism. The trachea was immediately removed, washed and immersed in buffered Ringer-Locke solution — pH 7.2. In this solution cilia remained active for at least 16 hours. The test was always started within two hours after the death of the rabbit. Rings of the trachea (one-third to one-half of the entire length) were immersed in the test solution at room temperature. At intervals strips of mucosa were cut from the trachea and examined under the microscope for evidence of ciliary activity. The time between the immersion of the trachea in the solution and the preparation of the last active strip was noted, as well as then taken as the mean of these two times. Since the average interval between the preparation of the two test strips was six minutes, there remains an undetermined interval of ±3 minutes for each recorded survival time.

"For the purpose of control with respect to the components in the product (dye and aromatics and sodium sulfite), a solution prepared without sulfite and a solution containing the sulfite but not the dye and the aromatics were tested parallel to the sample of the product.

"While no effect was observed in the living rabbit (surgical preparation using reflecting microscope) on the motility of the cilia of the exposed maxillary sinus after several hours' continuous application of the product, the mean duration periods of  $38.4\pm3.0$  minutes for ciliary activity of excised tracheal rings in solution containing the product,  $36.4\pm2.3$  minutes in solution containing the sulfite only, and  $34.6\pm1.9$  minutes in the solution containing no sulfite, are considered very satisfactory under the rather drastic conditions of this type of experiment. The results fail to show any significant differences in inhibiting effect on ciliary motility among the three solutions, i.e., neither the dye and aromatics nor the sodium sulfite in the product significantly influence the action of the product on ciliary motility. We have observed in other similar experiments that some of the commonly used nasal sprays either kill the cilia or inhibit motility almost instantaneously."

#### TOXICITY REPORTS.

A toxicity test worked out by Chen<sup>3</sup> at Eli Lilly Laboratories by intravenous injection in mice shows results indicating a low toxicity as follows:

Dose mgm./kgm.	Number Died Number Used	LDso±S.E. mgm./kgm.
560	0/8	
620	0/8	
700	1/8	
800	1/8	968.7 ± 38.7
900	2/8	
1,000	5/8	
1,100	5/8	
1,250	8/8	

# BACTERIOSTATIC AND SELF-STERILIZING PROPERTIES OF D. O. E. SULFA.

(Report by The Medical Research Laboratory of Parke, Davis & Co.)

In a test for self-sterilizing properties of D. O. E Sulfa it was found that: "There is a gradual diminution of bacteria over a period of six hours, but about one-sixth of the total number inoculated still remains viable at this time."

D. O. E. Sulfa was also submitted to a co-operating university laboratory to determine if the action of sodium sulfathiazole against Staphylococcus aureus was in any way altered by virtue of its chemical combination with d1-Desoxyephedrine hydrochloride. It was found that "The average percentage inhibition of hemolytic Staphylococcus aureus in Tryptose broth by sulfathiazole (12.5 mgm. per cent) was 73.0, and by sulfathiazole (12.5 mgm. per cent). when combined with d1-Desoxyephedrine hydrochloride at pH 7.8 was 70.3."

#### SUMMARY OF CLINICAL EXPERIENCE.

In our own records of over 1,000 cases of nose, throat and ear infections, and in more than 150 cases of eye infections reported to us by Dr. Alfred Robbins, oculist, the following conditions have been treated:

Sinusitis, acute and chronic: Frontal; Maxillary; Ethmoid; Sphenoid Rhinitis, Pharyngitis, Laryngitis, Tracheitis, acute and chronic; Otitis Media Suppurative, acute and chronic.

In acute sinusitis, office treatment included spraying the nasal membranes with 1 per cent solution of cocaine followed

by insertion of tampons medicated with approximately 20 minims of D. O. E. Sulfa, and left in place for 20 to 30 minutes. This accomplishes a very complete shrinking of the congested mucous membrane just short of that noticed with the use of adrenalin, yet without blanching, sneezing or subsequent swelling.

For home treatment patients were instructed to use spray or drops with sufficient frequency to keep the nose open. At the beginning of treatment this often necessitated using spray or drops at five-minute intervals, usually two or three times, until the deeper tissues in the nose were reached.

Chronic sinusitis was treated by irrigating the affected sinuses and following with the instillation of the solution into the sinuses, and the use of spray or drops at home.

Acute pharyngitis and laryngitis were treated by spraying the nose and throat and, in office treatments, also the larynx and upper trachea.

Acute suppurative otitis media was treated by myringotomy and medicated tampons in office treatment, and by drops in the ear and nose and in the epipharynx by the patient at home.

Chronic suppurative ears were treated by cleaning thoroughly with peroxide, followed by insertion of tampons; home treatment consisted in the prescribed use of drops.

This type of treatment we have found safe and effective.

# SAFETY AND EFFECTIVENESS IN SPECIAL CASES.

Membranous Laryngitis of Alpha Streptococcic Origin: Patient's blood count showed leucocytes, 3.300, following oral administration of six tablets of sulfadiazine over a period of 12 hours. D. O. E. Sulfa was used as a spray in the nose, throat and larynx q. 1 h. The following day the leucocyte count had risen to 5,300, and the next day to 7,000, with clearing of the membrane in the larynx.

Acute Infectious Mononucleosis with Acute Alpha Streptococcic Membranous Tonsillitis: The patient was seen at the hospital on the twelfth day of the disease. Temperature was 104°; leucocytes, 14,800; polynuclears, 14%; lymphocytes, 83.5%. Sulfathiazole orally, with local use of D. O. E. Sulfa,

brought the temperature to normal on the third day. Membrane which had covered the tonsil and part of the pharynx with beginning dyspnea disappeared.

#### UNFAVORABLE REACTIONS.

Two unfavorable reactions occurred during the course of our D. O. E. Sulfa therapy; one a local skin reaction; the other, a rise in temperature. Both patients were allergic to the sulfonamides.

#### CLINICAL OBSERVATIONS.

In acute colds D. O. E. Sulfa treatment resulted in rather prompt relief, and the duration of the infection was apparently shortened. This was also true in acute sinusitis, with less tendency to become subacute or chronic.

Many cases of chronic sinusitis reacted favorably where formerly surgery would have been indicated. There is no intention to suggest that D. O. E. Sulfa therapy is a cure, or that it substitutes for surgery where massive pathology of the membrane or bone exists, but indications are that it will greatly reduce the number of sinus surgeries that will become necessary.

Acute suppurative otitis media has been a much less frequent complication. Chronic suppurative otitis media that has resisted other forms of treatment has cleared up without a radical mastoid.

In children the treatment has been especially effective, particularly where the nose was blocked from colds and acute or chronic sinusitis. Packs used in the swollen nose opened it up and gave relief without discomfort, so that child-patients overcame fear of treatment.

For elderly people, and in systemic involvements where surgery is contraindicated, the therapy has offered a form of treatment that has produced considerable relief.

#### SUMMARY.

A stabilized solution of sodium sulfathiazole with d1-De-

soxyephedrine hydrochloride shows the following therapeutic characteristics:

- 1. It is apparently an effective bacterial agent for treatment of infections of the upper respiratory tract.
  - 2. It has a relatively low toxicity.
- 3. It has prompt and prolonged vasoconstrictor action without side-effects.
- 4. It has a comparatively favorable influence on ciliary motility.
- 5. Histopathological reports show that it does not injure the mucous membrane.

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# RHINOLOGY IN CHILDREN. RESUME AND COMMENTS ON THE LITERATURE FOR 1942.

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GENERAL ARTICLES ON ACCESSORY SINUS DISEASE IN CHILDREN.

Dowdeswell<sup>1</sup> reviews 60 cases of common cold seen in private practice and concludes that infections of the accessory nasal sinuses are prevalent in childhood as well as in adult life and are often diagnosed as recurrent colds.

Case histories and bacteriological findings suggest that apart from unmistakable cases of sinusitis, many are only mild and others have exacerbations of a chronic latent infection with possibly long quiescent periods; and that primary mild sinusitis may remain as a latent infection. The possibility of sinusitis should be seriously considered and the sinuses investigated in any case of pyrexia of unknown origin, influenza or febrile catarrh.

Shannon<sup>2,3</sup> calls attention to the fact that orthostatic or postural albuminuria in children is a frequent accompaniment and apparently a result of nasal sinusitis, especially of a subacute or chronic type; therefore, such albuminuria must be viewed with much more concern than has been the custom heretofore.

Bowers<sup>4</sup> discusses the dilemma of a young rhinologist who, from listening to the discussions of his elders and from perusal of the literature, endeavors to determine his own procedure in the diagnosis and treatment of sinusitis. He advises the young rhinologist to study all the methods of treating sinusitis; note the advantages and disadvantages of each, and learn to adapt each one to the individual patient. What is ideal for one will prove inadvisable for another. He is not to be too easily discouraged by adverse or contradictory reports. One patient differs from another as widely as one treatment from another; individual treatments vary as greatly as individual nasal structures. Remembering that both the case

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history and the type of patient have a bearing on the situation, the rhinologist must learn to select the most satisfactory type of treatment for the case at hand. No part of the anatomy is less understood by the general practitioner than the nose, and little time is spent by the rhinologist in explaining to him the results to be expected from any given procedure. Frequently a bad choice of operation is made. All this leads to misunderstanding. The young rhinologist requires serenity to leave alone what should be undisturbed, courage to do what should be done and wisdom to know one from the other.

### FRONTAL SINUSITIS, ITS COMPLICATIONS AND TREATMENT.

Boies<sup>5</sup> in an illustrated article on acute frontal sinusitis states that simple trephined drainage of the involved sinuses should be entirely through the sinus floor and should be performed early. His argument is supported by case reports on four patients, three of whom were children.

The majority of cases of acute frontal sinusitis resolve under conservative treatment. Such treatment usually consists of rest in bed, general medical support and care, shrinkage of the nasal mucosa, particularly in the middle meatus of the involved side, and the local application of cold or heat. Removal of the anterior tip of the middle turbinate is practiced by some rhinologists and is relatively conservative as it is easily accomplished and does not necessarily impair future nasal function.

The advent of the sulfonamide compounds has furthered the cause of conservation; however, a growing experience in the use of those drugs indicates that their action is not as effective in inflammatory bone lesions as in the soft tissues and when an empyema or abscess forms, it is still important to drain pus when feasible.

When there is definite and continued improvement in the fever and headache of an acute frontal sinusitis, rhinologists usually have no cause for concern. When, however, the fever persists and the headache is not relieved it is probable that drainage is inadequate. If there develops an actual edema of the upper eyelid of the involved side a grave danger signal is present to denote an actual spread of the inflammation without the walls of the involved sinus. The complications of

frontal sinusitis which are most severe are osteomyelitis and abscess within the cranium.

The pathology of this spread is now well understood. When drainage from the infected frontal sinus is not free, the pus under pressure causes a diminution of blood supply which predisposes to necrosis of the mucous membranes and thrombosis of the perforating veins. There follows a thrombosis of the diploic veins with a spread of the organism. Pus and granulations fill the diploe. Osteal necrosis occurs and the emissary veins may carry the infection through either or both tables of the skull.

Three procedures may be considered: 1. intranasal enlargement of the nasofrontal duct; 2. external trephine; 3. external operation on the sinus with the removal of grossly diseased bone and lining membrane combined with enlargement of the nasofrontal communication.

The first method is a relatively blind procedure. Because of this fact it often fails to provide the necessary drainage safely and adequately.

The second method would seem to be soundly conceived and based on an old and correct surgical principle; however, it has not been a satisfactory method in the experience of some rhinologists. The probable reasons for this form the background of Boies' paper and are fully discussed.

The third method has been widely used, the danger of inciting an osteomyelitis is now well appreciated, and this fact has caused a more conservative attitude towards radical surgery in the presence of acute inflammation.

The external trephine can fail to accomplish its purpose only if it does not provide adequate drainage or in that it is not a safe procedure. Adequate drainage should be provided if the frontal sinus is opened before the pressure has been in effect long enough to cause a necrosis and thrombosis which is part of the pathogenesis of complications of acute frontal sinusitis. The time element, therefore, seems to be important in the adequacy of this type of treatment. This is illustrated in the case reports.

The external trephine cannot be considered safe if it is conducive to the development of an osteomyelitis. The essen-

tial point is that cancellous bone may be present in the anterior wall of a frontal sinus and that surgical opening through this type of bone disposes towards involvement of the bone by the inflammation; therefore, when external drainage is indicated the approach should be made through the sinus floor where these dangers are greatly minimized. There is, however, some danger here if the opening is made anterior to a line extended upwards from the posterior lacrimal crest.

The author quotes Crowe, who recommends that in the handling of an acute frontal sinusitis needing surgical intervention this simple form of drainage is the first step. The mucous membrane of the sinus and the nasofrontal duct must not be curetted or disturbed in any way at the first operation. A small rubber tube is left in the external opening and the sinus irrigated with normal salt solution at frequent intervals. If the edema in the nasofrontal duct subsides sufficiently to allow the irrigating fluid to flow out through the nose, the progress as regards complete cure without operation is good.

Dill<sup>6</sup> reviews 10 consecutive cases of osteomyelitis of the frontal bone, all of which occurred before the advent of effective chemotherapy. Four of the patients were between 10 and 15 years of age.

He states that rhinologists are divided into two schools of thought as regards treatment: one argues for conservative and the other for radical surgery. Blair and Brown strongly advocate conservative treatment. They advise early drainage, allowing the virulence of the infection to subside; the removal of sequestra as they separate; and the later removal of the edges of all live bone that overhangs, so that soft tissue may drop in and fill the defects. Furstenburg, Mosher and Judd advise wide radical resection of both the inner and outer tables of the skull, well beyond the limits of the disease, so as to include the area of thrombosed diploic veins.

Dill's 10 cases of osteomyelitis were all of the localizing type, and a conservative type of treatment was carried out on all of them. A simple incision was made over the area of fluctuation and a drainage tube inserted. The acute infection was allowed to subside and sequestra were removed as they separated. Vaccines were given to two patients preoperatively, and transfusions administered to several patients before operation. When the general condition of the patient

warranted an operation, and the local infection appeared to have subsided, the frontal sinus was opened externally, diseased bone, pus and infected mucous membrane were removed and drainage provided into the nose. The mortality was two cases, or 20 per cent. One patient had an actinomycosis infection and died of a brain abscess, from which this fungus was isolated at autopsy; the second patient had previous operations on the frontal, ethmoid and maxillary sinuses, and the osteomyelitis was secondary to a second frontal operation. The patient developed bilateral and parietal abscesses which were incised and drained, but the patient succumbed to bronchopneumonia and leptomeningitis.

Dill concludes that the occurrence of osteomyelitis in cases of frontal sinus infection is still a problem. It is a serious complication and much more so when it occurs postoperatively. Perhaps chemotherapy may lessen the frequency of its occurrence and prove of value not only in the treatment but also in reducing the incidence.

Hanley reports in detail frontal sinusitis in a boy aged 14, which was followed by very extensive osteomyelitis and severe meningitis but which terminated satisfactorily with almost complete regeneration of the skull defects.

Coates and Hoffman<sup>s</sup> report frontal sinusitis in a boy aged 12, which was treated by external operation, the use of a sulfonamide compound locally, minimum drainage, and immediate closure of the wound without intranasal drainage.

The original infection occurred following swimming in the ocean. Ten days after the swimming episode the patient developed massive edema of the right eyelid and forehead and the headaches which had been severe became less. Pus was evacuated by an incision through the right eyebrow. This was followed by recovery, except that a fluctuating mass remained in the right frontal region, so the patient was kept under observation. In a little more than five months after the original attack, operation was advised because tenderness and more swelling over the right frontal with inflammation of the scar of the drainage incision developed. A radical frontal operation was performed, the wound was packed with sulfathiazole powder, and an obliterating closure was made. Since the nasal frontal ducts or passages were not disturbed

the postoperative course was quite uneventful, and three months after the frontal operation the site of operation was normal in appearance.

The case is remarkable for several features which the authors report and discuss briefly:

- 1. The length of time elapsing between the original infection and the operation, with no general symptoms for nearly four months. During all of this time there was a large area of fluctuation over the right brow but at no time any nasal discharge. Probably the chemotherapy administered at the onset of the disease cleared up the infection in the sinuses after perforation had occurred and had also limited its spread to the diploic bone, which was finally sealed off by the sclerotic process observed in the later X-ray studies.
- 2. The presence of an osteomyelitis of the anterior plate (which could have taken place only if this plate was diploic) and the destruction of the outer cortex, the inner plate of the outer table remaining intact. There were several sequestra observable in the X-ray plates representing the remnants of the cortex.
- 3. The mehod of treatment and its results. A classical external frontal sinus operation was performed on both frontal sinuses, with beveling of the bony edges, preserving most of the supraorbital ridges, but removing the chronically inflamed and infected mucosa. Since no secretion was present, the nasal frontal ducts were normal in appearance; there was and had been no nasal discharge and there was no intranasal pathology, the ducts were not disturbed. The entire cavity was filled with sulfathiazole crystals and a fenestrated drainage tube passed through the cavity to exit at the lateral margins of the skin wounds above the external canthi. Except for these openings the entire skin wound was closed accurately. The results have, at the least, exceeded the expectations of the authors.

Fred<sup>9</sup> reviews 40 cases of acute fulminating osteomyelitis of the frontal bone occurring in the wards of the Massachusetts Eye and Ear Infirmary during the years 1931 to 1941. He does not include chronic cases, traumatic cases, cases which on admission presented a draining fistula, or sinusitis cases which subsequently developed osteomyelitis after sinus surgery. The youngest was 4 years of age.

Osteomyelitis is a disease of the young. There were six cases in the first decade; one-half of the cases in the series occurred during the second decade of life.

The author is convinced that chemotherapy will surely modify, even revolutionize, the treatment of osteomyelitis. The greatest use of chemotherapy will no doubt be in the prevention of the disease, providing two conditions are satisfied. First, the sulfadiazine must be used early in the disease and in adequate doses; the blood level should be kept at no less than 20 mg, per cent (it is conceivable that a lower concentration might suffice) for optimum results during treatment in the early stages. Second, incision and drainage through the floor of the frontal sinus along with chemotherapy must be instituted very early in the disease. An incision similar to the one usually made for an external ethmoid exenteration, but much smaller, should be made, and the periosteum separated only enough to allow removal of a small part (1 cm.) of the floor of the frontal sinus for drainage of pus. Extreme care should be exercised not to traumatize, separate or suck out the mucous membrane lining the frontal sinus. No ethmoid cells should be removed even though the X-ray shows them involved. The best plan is to do as little as possible in an operative way consistent with free drainage from the frontal sinus. The maxillary sinus on the same side should likewise not be irrigated or operated upon at this initial stage of the disease. If these two conditions are satisfied, Fred feels that most cases of potential osteomyelitis of the frontal bone will be prevented. Chemotherapy alone (that is, without incision and drainage), in his opinion, is not enough in the average case, though no doubt some patients will recover on chemotherapy alone.

He concludes that the operation for removal of the frontal bone will be used in the future only on those rare occasions where proper prophylactic measures have not previously been used — which is another way of saying that the operation — as a method of choice — is on the way out.

# CELLULITIS OF THE ORBIT FOLLOWING SINUSITIS.

Wallner<sup>10</sup> presents a table giving the essential details regarding 10 cases of orbital cellulitis, of whom three were children, aged 7 years, 8 months and 15 months. Details regarding the predisposing cause of the symptoms, the sinus

involved, the bacteriology, the treatment and the course and results are given. Hot packs and local treatment to the nose were the essential treatment and recovery occurred in all three in periods varying from one week to one month.

The author states that there are several types of pathology which can cause the picture of orbital cellulitis: 1. a true cellulitis of the soft tissue of the orbit which may progress to phlegmon or abscess; 2. subperiosteal abscess outside the orbit proper and between the periosteum and bone; 3. thrombophlebitis of the orbital vein. Differentiation from a unilateral cavernous sinus thrombosis may be difficult or impossible. Venous stasis is important in the production of the clinical picture. Conservative measures will be sufficient for many of these cases.

Treatment aims at prevention of a central extension and cure of the orbital infection, as well as a cure of the causative sinusitis. Most standard texts and older articles advise surgery and incision and search for an abscess and radical exenteration of the sinus. Drainage of an abscess seems advisable, but the difficulty is in knowing when pus is present, as it may be deep and difficult to diagnose. If the pus is not found beneath the periosteum it is not likely to be found in the orbit proper, and trauma here, caused by searching for it, may be dangerous. The author considers that there is much to recommend conservative measures. Chemotherapy, hot packs, therapeutic X-ray and local shrinking in the nose will be sufficient in many instances. Infants and patients whose condition is due to scarlet fever have an especially good chance of recovery by these means.

### RHINITIS CASEOSA.

Farrior<sup>11</sup> describes the course and treatment of rhinitis caseosa. This rare type of unilateral nasal disease is characterized by the accumulation in the nose and paranasal sinuses of an extremely offensive cheese-like mass, by the presence of a seropurulent nasal discharge and other manifestations of chronic suppurative sinusitis and, lastly, by intranasal and frequently external deformities which result from pressure exerted by the caseous mass.

The patient, a farmer's son, aged 13, had the characteristic deformity of the face; that is, unilateral widening of the

bridge of the nose, with a malformation extending toward the malar eminence. This area was not reddened. There was no tenderness or crepitation of the underlying bony structure. One nasal vestibule was completely filled with mucopurulent discharge. Patient cleansing followed by nasal irrigation produced about an ounce of very offensive, greenishgray, putty-like material. This mass had completely filled the cavity, producing pressure changes on all walls and in all directions. The nasal septum had been pushed completely over to one side, resulting in almost complete obstruction of the otherwise normal left nasal chamber. The right middle turbinal was very small and was pasted against the lateral wall of the nose. The right inferior turbinate had been pushed downward against the lateral wall of the nose. The right frontal and maxillary sinuses were dark on transillumination, and roentgenographic studies disclosed diffuse clouding of all the paranasal sinuses on the right side.

A polypoid mass on the anterior end of the right middle turbinate did not resemble the nasal polyp found in cases of allergic rhinitis; as there was no increase in the number of goblet cells, the basement membrane was not widened, and the infiltration of eosinophiles was less than 10 per cent of the cellular element.

During the first four days of hospitalization the patient was given frequent irrigations of potassium permanganate. The offensive odor which had been present for many months completely disappeared in this brief period. A few days later the right maxillary sinus was given adequate intranasal drainage through a window in the inferior meatus. Probing through this window and irrigation of the right antrum disclosed no caseous mass and only moderate thickening of the lining mucous membrane.

After the right antrostomy the patient was given daily irrigations of the antrum. The sinus infection subsided. Four months later there was no evidence of reformation of the caseous mass. The facial deformity was still present. Except for being slightly oversized, the appearance of the right nasal chamber was nearly normal. The septum was still greatly displaced to the left. The middle and inferior turbinates on the right side had returned to their proper positions and the mucous membrane was regaining its smooth, pink appear-

ance. This rapid recovery, once the caseous mass is removed, is one of the characteristness of rhinitis caseosa as it is presented in the literature. It demonstrates that radical operation on the sinuses is not indicated simply because there is diffuse clouding of all the paranasal sinuses and that these sinuses will return to normal if they are given an opportunity to drain properly.

# OSTEOMYELITIS OF THE SUPERIOR MAXILLA.

Barker<sup>12</sup> describes in detail acute osteomyelitis of the superior maxilla in an 18 months old child who made a satisfactory recovery. It was remarkable in that first there was an absence of palatal swelling throughout the illness and, second, that the teeth particularly involved were the incisors and canine, the first molar being quite unaffected. He points out that drainage by the sublabial approach was inadequate and thinks that an incision below the inner canthus and counter drainage into the nose would have shortened the illness and promoted more rapid healing.

#### TREATMENT OF ACCESSORY SINUS DISEASE.

It is common practice for a patient to purchase a dropper bottle of solution of one of the common vasoconstrictors, treat his cold and then put the bottle away in the family medicine cabinet. It is subsequently brought out thereafter when any member of the household has a stuffy nose. The dropper is inserted into the offending nostril and then put back into the bottle. In these words Gompertz and Michael<sup>13</sup> describe the malpractice which causes the commonest disease in rhinology, and it is hoped that their article will be widely read. Usually the dropper has been inserted well into the nostrils; therefore, the questions arise as to the possibility of nosedrops being a source of transmission of infection from one member of the family to another and of a future "cold" being complicated by the use of nose-drops contaminated from a previous "cold."

The question of sterility of solutions for intranasal use is important and there is an answer. The answer does not lie in avoiding the issue by the use of stronger antiseptics; it lies in sterile solutions correctly dispensed and correctly used.

The points made by the authors are as follows:

- Fresh nose drops as they are dispensed are probably sterile.
- 2. The usual content of preservative or antiseptic is insufficient to maintain sterility in the face of repeated contamination.
- 3. Many popular intransal vasoconstrictor solutions have no bactericidal effect on staphylococcus aureus hemolyticus.
- 4. Repeated contamination of nose-drops results in their supporting living bacteria. This is probably due to the addition of mucus and other debris from the nose.
- 5. The use of contaminated dropper-bottle contents by others or in subsequent colds is not without risks.
- 6. Since sufficient antiseptic to insure sterility under circumstances of repeated contamination would make a solution unfit for intranasal use, owing to discomfort from mucosal irritation and damage, the way to progress would seem to be towards solutions prepared, sold and used in such a manner as to avoid contamination.

The main purpose of the paper is to condemn two practices that are widespread among the public and are at times fostered unintentionally by physicians. These are:

- 1. The use by a patient of someone else's dropper bottle of nose-drops; and
- 2. The use by a patient of dropper bottle nose-drops that he has used during a previous infection of the upper respiratory tract.

In order to avoid the complications of these practices the physician should educate his patients to do one of two things: If they insist on buying dropper bottles of solutions they should buy very small ones, allow no one else to use them and throw them away at the conclusion of their current infection; however, the safer and better method is to buy sterile drops containing no antiseptic in a plain screw-capped bottle. Instruction is given to pour out the amount needed for treatment and replace the screw cap at once. Never pour anything back into the original bottle and never put a dropper or anything else into it.

In reply to a correspondent the *Jour. A. M. A.*<sup>14</sup> states that when a 5 per cent solution of sulfathiazole sodium in distilled water is used as a spray in the nose or throat, there is a rapid dilution of the original solution together with a decrease in its alkalinity due to the buffering action of the nasal mucus and saliva, so that the chance of irritating effects being produced is decreased; but when a 5 per cent solution is used as a spray at frequent intervals, the patient may complain of a sensation of heat and burning in the area to which the spray of the solution of sodium sulfathiazole has been applied. Fletcher has reported that necrosis of the lining of the maxillary sinus occurred after irrigations of the sinus with solutions of sodium sulfathiazole for three weeks. Solutions of the sodium salt of sulfathiazole may decompose if exposed to light over several days; for this reason when sprays of sodium sulfathiazole solution are being employed, prescription should be written for a two days' supply in order that a decomposed solution is not used by the patient.

The *Journal* stated that so far there had been no studies conducted on the effect of sprays of sodium sulfathiazole on the cilia of the nasal passages. A final conclusion on that point could not be reached at present because of the lack of experimental work.

Until the results of such investigations are available it would seem that a considerable degree of caution should be used in the application of alkaline solutions of sodium sulfathiazole to the nasal mucous membrane.

Merica<sup>15</sup> describes his own experience in the use of a 5 per cent solution of sodium sulfathiazole by means of nasal tamponage. The packs were inserted, for the most part, in the middle meatuses following the application of 5 per cent cocaine and were left in place from 15 to 30 minutes. The solution was used on more than 300 patients and one patient had more than 75 applications over a period of six months. These patients were observed closely and at no time did he detect any sloughing of the nasal mucosa.

There were some patients who did not tolerate this drug, as was manifested by reactions resembling an allergic rhinitis following its use. For the most part, patients were impressed with the fact that there was very little reaction following the treatment.

He found that when the solution had been made up for a few days it became quite irritating, as evidenced by sneezing and much turgescence a few minutes after application. This was also corroborated by patients who were given solutions to use in the prescribed atomizers at home.

Futch, Rosenbold and Stewart<sup>16</sup> describe the effect of solutions of sulfathiazole in 5 per cent concentration when applied to the nasal mucous membranes of rabbits. They conclude that a 5 per cent solution of sulfathiazole sodium sesquihydrate is injurious to the nasal mucous membrane of rabbits. The cilia and superficial layers of columnar cells, to a large extent, are destroyed, and even after one week recovery does not take place.

The solution used was described as isotonic. The authors remark that the use of the term "isotonic" may be somewhat misleading to those interpreting the term "isotonic" as meaning nonirritant. They express the hope that soluble combinations of the sulfonamide without caustic properties may yet be produced.

Boussard and Fry<sup>17</sup> have published two papers describing the cure of chronic nasal diphtheria carriers by the use of sulfanilamide. In a report to the Medical Research Council they reported their observations of two to six months' study of nose and throat swabs from diphtheria patients and their contacts. They had shown that nasal infection with hemolytic streptococci was very common in cases of nasal diphtheria. They had formed the opinion that hemolytic streptococcal infections of the nose in cases of nasal diphtheria materially prolonged the period of carrying.

They have published a second paper reviewing data collected over an additional 11 months.

The results of swabs from 388 diphtheria patients in hospital have been analyzed. One hundred seventeen of them had a double infection with C. diphtheriae and hemolytic streptococci in the nose, and the average stay in hospital for those cases was 87.5 days, more than twice the average for all cases without such an infection.

Sulfanilamide powder was administered intranasally to 26 children with a heavy double nasal infection who had been positive for periods ranging from four to 23 weeks. In 24

the nasal infection was abruptly and permanently ended by the first eight-day course of treatment. In the other two this result was achieved by a second course. In addition two nasal carriers with a double infection of 11 and 5 months' duration were treated outside hospital and cured.

It is concluded that the persistence of C. diphtheriae in the nose mainly depends on the associated hemolytic streptococcal infection which can be cleared up with sulfanilamide powder. Some of the results suggest that sulfanilamide has a direct action on C. diphtheriae.

Brighton, Snow and Friedman<sup>18</sup> state that the advent of short wave therapy on the therapeutic horizon in the past 10 years has brought forth exorbitant claims regarding its efficacy. They make a statistical analysis of 160 cases of acute and chronic sinusitis and of allergic rhinitis treated by short wave therapy in Vanderbilt Clinic in the past three years and summarize their conclusions as follows:

- 1. Short wave therapy is employed indiscriminately in many intranasal conditions in which it does little good and may do harm.
  - 2. It is of no value in allergic rhinitis.
- 3. Its application in acute sinusitis, even in conjunction with nasal shrinkage and irrigations, does not produce results superior to conservative nasal therapy alone.
- 4. In cases of nonpurulent sinusitis which present in general a poor prognosis, it is of definite benefit particularly in the relief of headaches.

#### ANATOMICAL ABNORMALITIES.

Kazanjian<sup>19</sup> states that congenital atresia of the choanae is a rare anomaly. Twenty-seven thousand eight hundred sixty-three nasal cases were seen in the Ear, Nose and Throat Department of the Royal Infirmary of Edinburgh during a period of 20 years and among these were only six cases of unilateral atresia and no bilateral cases. Sixty-two thousand two hundred twenty-eight cases at the Massachusetts Eye and Ear Infirmary during a 16-year period yielded 10 cases of atresia. of which four were right-sided, three left-sided and three were bilateral. This group of 10 cases forms the

basis of Kazanjian's report. In this series four had bony atresia, two had membranous atresia and in four the atresia was bony with a central membranous area.

The patients in whom the condition was unilateral had partial function of the nose and hence showed less marked symptoms than the bilateral cases. The author suggests that it was for this reason that tonsillectomy, septal deflection and adenoid and sinus operations had been performed, suggesting that the true condition had escaped diagnosis.

Bilateral occlusion in infants causes great difficulty in breathing and this has been reported as a frequent cause of asphyxia of the newborn.

The following points are helpful in making a diagnosis of congenital atresia:

- 1. There is complete obstruction of one or both sides of the nose with no other definite cause but a badly deviated septum, a foreign body or tumor.
- 2. The floor of the nose is covered with a collection of mucus secretion.
- 3. The passage of a probe into the nasopharynx is found to be impossible.
- 4. The posterior choanae by inspection or palpation will present a characteristic picture, which is illustrated.
- 5. An X-ray examination of the nose filled with an opaque oil is diagnostic.

The author describes his own method of dealing with the abnormality — gives three detailed case reports and provides ample illustrations.

#### MASSIVE HEMORRHAGE.

Mocley<sup>20</sup> reports seven cases of massive hemorrhage with one recovery and six fatalities. Five of the seven were in young children. Adequate case reports are given and he uses these in making a review of the available literature, showing that fatal hemorrhage is a fairly commonly reported complication of deep neck infection.

He concludes that bleeding from the nasopharynx or throat associated with peritonsillar or pharyngomaxillary infection is a danger sign that calls for immediate ligation. Bleeding from the ear if associated with throat or neck infection and swelling calls for immediate ligation of the carotid artery.

#### ATROPHIC RHINITIS AND OZENA.

Collum<sup>27</sup> in a long article, illustrated by seven plates, ably discusses the etiology of ozena. By oversight this article was omitted from the 1941 review of the literature. Four case reports are given. The discussion which follows is lengthy and valuable.

The conclusions are the result of a lifetime of observation of patients with ozena, together with a careful study and analysis of the observations and conclusions of the many rhinologists who have seen the end-result of a chronic purulent focus. This focus may be in the nasal cavity, the accessory sinuses or the postnasal space. His conviction is based on the brilliant observation of Bosworth that there is a purulent rhinitis of early childhood which results in ozena in from five to 10 years. Bosworth had an enormous clinical experience and apparently followed his patients through the stage of purulent rhinitis to the point at which the condition developed into atrophic rhinitis. The purulent rhinitis of childhood theory has the support of a large number of physicians who have confirmed it in their experience. There is almost unanimous agreement among rhinologists who keep careful histories that the beginning of discharge dates from an attack of an exanthem, diphtheria or epidemic influenza. The next step in logical sequence is to connect the purulent discharge with purulent sinusitis resulting from this attack.

A stumbling block to many authorities is the fact that ozena appears five times as often among females as among males. There are, of course as many cases of purulent sinusitis in boys as in girls. If the purulent sinusitis is the cause, why are there not as many cases of ozena in males as infemales? Collum's theory depends on the difference in habits of boys and girls. Boys are outdoor animals. They love fresh air and outdoor games that call for violent exercise and cause elevation of the blood pressure. The turbinal venous sinuses are filled with blood in a physiologic response to the increased temperature and the exercise, and a ravenous appetite is created. On the other hand, the girls of former generations lived

an indoor life. They liked to play with dolls and did nothing to raise their blood pressure. They lived in too dry an atmosphere, and their lack of fresh air and exercise reacted on their appetites so that they did not get the proper amount of nourishing food. All these things would make them a prey to the deficiency diseases which some physicians think are at the root of atrophic rhinitis.

The incidence of ozena has greatly decreased. There may be several factors involved. First, the population is receiving much more intelligent treatment of disorders of the nose and throat. Diseased tonsils and adenoids are being removed, and purulent sinusitis is being attended to. Second, much more intelligence is being shown in feeding children, which lessens the incidence of deficiency disease. Third, children lead a much more athletic, open-air life than they did formerly. This applies especially to girls.

Collum has a final word for rhinologists who do not believe that a purulent focus is the cause of atrophic rhinitis. When one takes into account the enormous number of patients who have been freed from their disgusting affliction by surgical drainage, why should not every patient with atrophic rhinitis be given the benefit of a careful search for such a focus? The fact that a purulent focus cannot always be found does not mean that such a focus is never the cause. Every patient should be given the benefit of a most painstaking investigation in an effort to locate the cause of the disease. His firm conviction is that ozena is a disease of children just as much as scarlet fever, measles, diphtheria and the exanthems and is inextricably bound up with them. When one can dispose of the purulent focus one can dispose of the crusts and fetor and let the unfortunate victim of ozena resume his place in society.

Safer<sup>21</sup> states that for a year and a half he has been treating a group of 20 cases of atrophic rhinitis with estrogenic substance. The nose is first cleansed of all crusts. These are detached with the aid of a bayonet forcep and a nasal spray, after which the patient blows his nose, evacuating the loosened crusts. The nasal cavities are then packed with large cotton pledgets which have been moistened with estrin. The pledgets are made as large as possible and have two threads about three inches long attached to them. The pledgets are

placed in the region of the middle meatus with the strings extending into the anterior nares for easy removal by the patient. The patient is instructed to leave the packs in place as long as possible. With the first two treatments he can retain this packing for only a few hours, but later most patients can keep the packing in place for as long as two or three days without discomfort. Patients were treated in this manner twice daily. After the packing is withdrawn they are instructed to use a warm alkaline nasal irrigation each day until they return for the subsequent packing. In addition they are given an estrin spray to use twice daily. The spray is regulated to deliver 0.25 cc. of estrogenic substance into each nostril. After improvement is noted the alkaline irrigations are discontinued and the estrogenic substance sprayed into the nose only once a day.

Improvement was noted within a few weeks after beginning this therapy. The crusts began to dissolve, and the mucosa became somewhat more pink in color.

The author states that there is no question among the patients as to their improvement, and almost all wish to continue the therapy. He concludes that estrogenic substances are a useful group of therapeutic aids in the treatment of atrophic rhinitis. He had had the opportunity of comparing cases under former methods of therapy and now treated with estrin and the results with estrin are striking. Twenty cases were treated with noteworthy alleviation of symptoms in all. It is the author's opinion that estrin therapy is merely palliative and not curative but should be given a very high rating in our therapeutic armentarium for the treatment of atrophic rhinitis.

[Editorial Note: There were no children in the series. The paper is included because this review has in past years abstracted articles on estrogenic therapy in atrophic rhinitis.]

Calderin, Lariu and Fernandez<sup>22</sup> advance the theory of ozena. They believe the atrophy to be the result of a neuritis of the trigeminus by a descending or an ascending process which attacks the ethmoidal fibres of the nasociliary branch of the ophthalmic nerve, or of the sphenopalatine nerve. The authors consider it necessary to influence the sympathetic in its action on the nasal fossa, thereby producing more lasting results. Two points are decisive in the treatment: One,

reducing the calibre of the abnormally wide and atrophic nasal fossa; two, modifying the nasal sympathetic in order to correct the trophic action. Barium oxide in petrolatum is injected into the nasal fossa and this is combined with roentgen therapy of the cervical region. There is no advantage in applying roentgen rays to lateral cervical fields; it is much more simple and rapid to resort to a frontal attack. This form of roentgen therapy has proven harmless. The irradiation was of medium penetration so as to stimulate the peripheral sympathetic.

#### FRACTURE DISLOCATION OF THE NOSE.

Salinger,<sup>23</sup> in 1941, contributed a comprehensive, amply illustrated article on injuries to the nose in children, which through oversight was omitted from the 1941 review of the literature. The article is noteworthy in that it is in disagreement with certain prevalent beliefs and certain statements frequently seen in textbooks. There are many of these points and the reader is referred to the original article lest this condensation give rise to misunderstanding.

It is Salinger's experience that physicians are inclined to minimize the real damage when a child's nose has been injured, because of failure to examine the nose thoroughly. They are misled by the smooth swelling and the apparent lack of signs indicating fracture or displacement, and as a rule their advice to the parents is to wait until the swelling has disappeared. He states that this is a tragic error, because by the end of a week or 10 days the malformation has already become fixed; the optimum time for intervention has passed, and the child is doomed to go through many years with a deformed nose before anyone will have the courage to undertake its correction. He states that operation for repair should be done at the earliest possible moment after the injury or as soon as the child's condition will permit. It is often difficult and indeed inadvisable to attempt reduction of the fracture during the first few days because the general condition of the child may be critical and the other injuries more threatening. Nevertheless, when the deformity is marked and obvious, no time should be lost in making a diagnosis and attempting the reduction.

He considers the roentgenogram most important. He considered it by all odds the most important means of diagnosis.

He admits that the bones of a child's nose are incompletely ossified and yet he believes that fractures can be demonstrated if roentgenograms are taken properly. It is important to remember that the tissues being examined are thinner than those of the adult and one should make due allowance by using a softer ray and shorter exposure than for an adult. It is essential that the overlying soft tissues show up in the pictures so that their relation to the bones can be clearly made out. He finds that the two best projections are the lateral and the Waters position.

The various types of external splint requiring application of a plaster cast to the head and application of pressure pads to the side of the nose have seemed to him to be too cumbersome for a child, and the pressure pads carry the danger of pressure necrosis. The through and through suture over lead plates may be effective in adults, but in several children for whom it was employed he found that the pressure marks persisted for a long time. He has been partial to the molded copper splint for a number of years, and since working out a method of insuring its remaining in place he has found it eminently satisfactory in children. A starched circular head bandage is applied rather firmly and permitted to dry thoroughly. This is usually done the night before or at least four hours before the splint is attached. Its purpose is to afford a fixed point to which the adhesive splint holding the splint in place may be attached. It is light, easily borne and in this respect much better than plaster of Paris or plastic material. A pattern of the nose must be made that will follow the inferior margins of the orbit closely and come down the sides of the nose on to the cheek, since it is important that the splint rest below the malar prominence and not directly on the nasal bridge. The remainder of the considerations regarding the application of the splint should be studied in the original article. The splint may stay in place for a number of days; the only reason for changing it will be that it gets very dirty. Unless the patient has pain or the splint seems to be out of place there is no need of changing it oftener than once in three or four days. In most cases it is needed for seven to 10 days. By that time the fragments have united sufficiently to be safe without any protection. He emphasizes that the employment of this procedure, in many cases, will prevent the development of a broad nose as a result of bending or spreading of the soft nasal bones. The continuous and gradual pressure over the sides of the nasal bridge counteract this tendency and eventually forces the bones to develop in their natural direction. It may be necessary to continue to use the splint for as long as three weeks, but he has never seen it do any damage providing it is carefully watched and adjusted according to the conditions present.

#### NEW GROWTHS.

Holmes<sup>24</sup> makes a review of the 15 cases of dermoid cysts of the nose that have been recorded at the Massachusetts Eve and Ear Infirmary during the past 20 years. Dermoid cysts may be present and conspicuous at birth but more commonly they do not reveal themselves until later in life. The most common age at which this group of cases was first observed was from 10 to 20 years. The reason for this is due to their microscopic structure. The walls of these cysts are usually comparatively thick and are lined with a squamous epithelium which contains hair follicles, sweat and sebaceous glands. All the elements of the normal skin are present. At birth these inclusion elements are very small and may be microscopic, but during growth the products which normally go through the surface of the skin, the hairs, desquamated epithelium, sebaceous and sweat secretions are entrapped within the center of the mass. This accumulation forms a core about which the epithelium proliferates and stretches. becoming larger and larger.

It is following this period of gradual accumulation that the tumor presents itself. These cysts may occur at any line of fusion of the embryo. Thus they are seen not only in the nose but also about the auricle, the orbit, the floor of the mouth, the anterior fontanel and the occipital protruberance.

Dermoid cysts of the nose usually start in connection with either the nasal or frontal bones so that even if a cyst presents itself at the tip of the nose, its stalk of origin will be found to extend to and make contact with either the nasal or frontal bone.

Taken as a whole, these cases presented a swelling of the nose which had been observed some time following the birth of the child. In some the swelling remained encapsulated and was retained beneath the skin. In others the sack had become

infected and had broken through the surface, creating a draining fistula. When this was the case, the attending physician had invariably incised the mass, curetted it, applied some caustic to destroy the lining epithelium and allowed the defects to close by second intention. The majority of their results was discouraging as the lining of the cysts had not been destroyed completely. Even a trace of remaining germinal epithelial tissue or gland structure is sufficient to recreate a new cyst; therefore, it is imperative to eradicate the cyst completely or establish a large drainage fistula which will carry away the products of proliferation.

The author gives in detail three case histories to illustrate the manner in which each particular problem was met. Excellent drawings accompany the article.

He concludes — a swelling within or beneath the skin of the nose, if not an abscess or sebaceous cyst, may very likely turn out to be a dermoid cyst. One must always be on the alert for a meningocele. Dermoid cysts must be completely removed before a cure can be obtained, as the slightest vestige of remaining cyst wall or glandular cells can cause the cyst to regenerate. These postoperative cysts inwardly become infected or break through the old incision, creating a draining fistula.

Priest and Boies<sup>25</sup> present reports of two extensive osseous maxillary tumors, one of which occurred in a child.

Only a few such cases have been reported and the treatment of these cases was contrary to the radical surgical therapy often advocated. The literature is briefly reviewed and covers the incidence and pathology.

The two cases reported were treated only by roentgen therapy. The diagnosis was established in each case by biopsy. Both were of the spongiose type of osteoma. Each involved the maxillary sinus and had expanded enough to disfigure the patient's face. The osteoma ceased to grow soon after treatment. The authors recognize that other factors than the radiation may have caused the cessation of growth. These tumors are known to start in childhood and have a tendency to stop growing in adult life. In the case reported below, 12 years have now gone since therapy and the patient is well.

A white female, age 14 years, during a dental examination in 1929, was found to have a swelling on the left upper jaw. The swelling had not been painful. The patient was unaware of its presence. The authors examined the patient six weeks later.

Examination revealed a smooth, hard outgrowth on the lateral surface of the left maxilla above the teeth. There was diffuse enlargement of the left cheek. Roentgenography revealed a dense bony mass encroaching upon the left maxillary sinus cavity. A tentative diagnosis of osteogenic sarcoma was made. Biopsy was not done, and 125 per cent skin erethema dose of deep roentgen therapy was given in three treatments over six days, in October, 1929.

The patient returned to the hospital in March, 1930. The tumor had increased slightly in size during the 18 months' interval but did not trouble the patient. A biopsy showed the tumor to be an osteofibroma. In two treatments over three days 115 per cent skin erethema dose of roentgen therapy was given over the left antrum.

The patient was re-examined in 1941. The mass had changed little during the 12-year interval. The radiologist commented that the appearance was typical of what is described as a sclerosing fibroma of bone which does not appear to be progressing.

A photomicrograph of the tissue from the patient, a roentgenograph, 12 years after diagnosis, showing replacement of part of the antrum cavity by bone together with thickening of the maxillary wall, and a photograph of the patient 12 years after the original diagnosis are given.

The patient is now a graduate nurse and carries on her work without symptoms from the tumor.

Berkove<sup>26</sup> reports adamantinoma in the floor of the right nostril in a child aged 5 years. This tumor is characterized by its slow growth and its recurrence after high voltage roentgen irradiation. Two pictures of histological sections are given.

The child was referred by a pediatrician because she had a suppurative swelling in the floor of the right nostril. A diagnosis of furuncle was made and roentgen therapy applied. The lesion disappeared completely after three treatments. Nine months later a mass was again noted. This was much more extensive, pushing forward the right ala nasi and the right portion of the upper lip and involving the nasal floor. The diagnosis of a malignant growth was considered and biopsy recommended. The mother wished to try high voltage roentgen ray therapy and several treatments were given. The mass again disappeared. Three months later the child returned with a growth larger than before. The tumor now seemed to involve the maxilla under the right ala nasi and extended inward to include the lateral wall and the floor of the nasal vestibule and the anterior portion of the inferior turbinals. The roentgenographic report was: "There is no evidence of involvement of the maxilla."

Four months later under general anesthesia a sublabial incision was made along the entire upper alveolar margin and the skin and mucous membrane were elevated, revealing a tumor. The neoplasm had its origin in the area above the right lateral incisor and involved the floor of the right nasa! vestibule. A dense fibrous capsule surrounded the mass, which could easily be separated from the surrounding tissue. The anterior wall of the maxilla was normal in appearance and was not included in the procedure.

Section showed an invading tumor composed of round, oval and spindle-shaped cells with a moderate number of mitotic figures. In some cases there was a pseudo-papillary structure. The tumor had a partial fibrous capsule and a dense fibrous stroma. The operative wound healed per primam in three weeks. The child was then given high voltage roentgen radiation to the area in an amount consistent with her age. She has gained about 10 pounds. The nasal floor has healed, as has the lateral wall, and appears normal. Time alone will tell whether a cure has been obtained.

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